



10

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Garcia-Blanco, Mariano A.
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<120> METHODS AND COMPOSITIONS FOR USE IN
SPLICEOSOME MEDIATED RNA TRANS-SPLICING

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<141> 2001-04-20

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<400> 45
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<210> 46
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<400> 50
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<400> 52
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<210> 53
<211> 24
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<220>
<223> Trans-spliced product containing humanchorionic
gonadotropin gene 6 sequences and Corynebacterium
diphtheriae toxin A sequence

<400> 53
gagatgttcc agggcgtgat gatg 24

<210> 54
<211> 127
<212> RNA
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<223> A, C, G or U

<221> misc_feature
<222> (57)...(70)
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gcugcag 127

<210> 55
<211> 127

<212> RNA
<213> Artificial Sequence

<220>
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<221> unsure
<222> (57)...(70)
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<223> Loop comprising a combination of 14 nucleotides

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nnnnnnnnnn aucguuaacu aaauaacuac uaacuggggug aacuucugua uuauucucga 120
gcugcag 127

<210> 56
<211> 127
<212> RNA
<213> Artificial Sequence

<220>
<223> PTM intramolecular base paired stem

<221> unsure
<222> (57)...(70)
<223> A, C, G or U

<221> misc_feature
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<223> Loop comprising a combination of 14 nucleotides

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gcugcag 127

<210> 57
<211> 132
<212> DNA
<213> Artificial Sequence

<220>
<223> Trans-spliced product containing human chorionic gonadotropin gene 6 sequences and Corynebacterium diphtheriae diphtheria toxin A sequences

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tccattcaaa aa 132

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<223> Artificial Sequence derived from Escherichia coli
lacZ gene

<400> 58
gaattcggta ccatgggg 18

<210> 59
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Artificial Sequence derived from Escherichia coli
lacZ gene

<400> 59
cgtttacagg taagaggatc ctccggaggg ccc 33

<210> 60
<211> 30
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<220>
<223> Artificial Sequence derived from Escherichia coli
lacZ gene

<400> 60
tggtgtcaaa aataataagt taacaagctt 30

<210> 61
<211> 25
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<220>
<223> Trans-spliced product containing Escherichia coli
lacZ gene sequences and human chorionic
gonadotropin gene 6 exon 2 sequences

<400> 61
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25

<210> 62
<211> 286
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<220>
<223> Trans-spliced product containing Escherichia coli
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acgggcaacc cgtggtcggc ttacggcggg gattttggcg atacgccgaa cgatcgccag 240
ttctgtatga acggtctggt ctttgccgac cgcacgccgc atccag 286

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<220>
<223> Trans-spliced product containing Escherichia coli
lacZ gene sequences

<400> 63
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ttcggccacg gtgccc 196

<210> 64
<211> 420
<212> DNA
<213> Artificial Sequence

<220>
<223> Trans-spliced product containing cystic fibrosis
transmembrane regulator-derived sequences and
His-tag sequence

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tgatgattat gggagaactg gagccttcag agggtaaaat taagcacagt ggaagaattt 180
cattctgttc tcagttttcc tggattatgc ctggcaccat taaagaaaat atcatctttg 240

gcggccgccca ctgtgctgga tatctgcaga attccaccac actggactag tggatccgag 300
 ctcggtacca aggttaagtt taaaccgctg atcagcctcg actgtgcctt ctagttgccca 360
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 <213> Artificial Sequence

<220>
 <223> Splice junction sequence

<400> 65
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<210> 66
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 <212> PRT
 <213> Artificial Sequence

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<400> 66
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<210> 67
 <211> 15
 <212> DNA
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 <223> Artificial sequence comprising sequences derived
 from Esherichia coli lacZ gene sequences

<400> 67
 ggagttgatc ccgtc

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<210> 68
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 <212> DNA
 <213> Artificial Sequence

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 <223> Artificial sequence comprising sequences derived
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<210> 69
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<223> Binding domain of PTM

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<220>
<223> Spacer sequence of PTM

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<223> Branch point, pyrimidine tract and acceptor splice
site of PTM

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tactaactgg tacctcttct tttttttttg atatcctgca gggcggc

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<210> 72
<211> 70
<212> DNA
<213> Artificial Sequence

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<223> Donor site and spacer sequence of PTM

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gatccaccgg 70

<210> 73
<211> 260
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ctccatttct cccataatca tcattacaac tgaactctgg aaataaaacc catcattatt 240
aactcattat caaatcacgc 260

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<210> 75
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actcagtgtg attccacctt ctc 23

<210> 76
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<400> 76
gacctctgca gacttcactt ctaatgatga ttatgg 36

<210> 77

<211> 33
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<210> 78
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<400> 78
ctagggttac cgaagtaaaa ccatacttat tag

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<210> 79
<211> 35
<212> DNA
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<220>
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<400> 79
gcatgggttac cctgcagggg ctgctgctgt tgctg

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<210> 80
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
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<400> 80
ctgaaagctt gttaaccagc tcaccatggt ggggcag

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<210> 81
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Binding domain of PTM molecule

<400> 81
acccatcatt attaggtcat tat

23

<210> 82
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 82
gatcaaattct gtcgatacctt cc

22

<210> 83
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 83
ctgatccacc cagtcccatt a

21

<210> 84
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 84
gactgatcca cccagtcca ga

22

<210> 85
<211> 52
<212> DNA
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site.

<221> misc_feature
<222> (7)...(30)
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<221> unsure
<222> (7)...(30)
<223> A, C, G or T

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<210> 86
<211> 71
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 86
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tatgatgaaa a 71

<210> 87
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 87
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acgccg 66

<210> 88
<211> 192
<212> DNA
<213> Artificial Sequence

<220>
<223> PTM sequence

<400> 88
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tccggccgca tcagcttttg cagccaattc agttggatca tgcccggtac catcaaggag 120
aacataatct tcggcgtcag ttacgacgag taccgctatc gctcggtgat taaggcctgt 180
cagttggagg ag 192

<210> 89
<211> 25
<212> DNA
<213> Artificial Sequence

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<223> Oligonucleotide

<400> 89

gagcaggcaa gacgagcttg ctcat

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<210> 90

<211> 28

<212> DNA

<213> Artificial Sequence

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<223> Oligonucleotide

<400> 90

gagaacataa tcttcggcgt cagttacg

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<210> 91

<211> 30

<212> DNA

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<223> Oligonucleotide

<400> 91

gtcagttgga ggaggacatc tccaagtttg

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<210> 92

<211> 192

<212> DNA

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<220>

<223> Oligonucleotide

<400> 92

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<210> 93

<211> 27

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<220>

<223> PTM sequences

<400> 93
aaatatcatt ggtgttttctt atgatga

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<210> 94
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<212> DNA
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<220>
<223> Oligonucleotide

<400> 94
ccaactagaa gaggacatct ccaagtttgc

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<210> 95
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<220>
<223> Oligonucleotide

<400> 95
atgatcatgg gcgagttaga accaagtgag

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<210> 96
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<220>
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<400> 96
aaaatatcat ctttggtggt tcctatg

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<210> 97
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 97
ccaactagaa gaggacatct ccaagtt

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<210> 98
<211> 21
<212> DNA

<213> Artificial Sequence

<220>

<223> 5' splice site

<400> (98

cgtttacagg taagtggatc c

21

<210> 99

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' splice site

<400> 99

ctgcagggcg gcttcgtcta ataatgg

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<210> 100

<211> 65

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<223> Sequence from trans-splicing domain

<221> unsure

<222> (7)...(18)

<223> A, C, G or T

<400> 100

gctagcnnnc cgcggnnnta ctaactggta cctcttcttt tttttttgat atcctgcagg 60
gcggc 65

<210> 101

<211> 1584

<212> DNA

<213> Artificial Sequence

<220>

<223> CFTR PTM

<400> 101

atgcagaggt cgcctctgga aaaggccagc gttgtctcca aacttttttt cagctggacc 60
agaccaattt tgaggaaagg atacagacag cgcctggaat tgtcagacat ataccaaatc 120
ccttctgttg attctgctga caatctatct gaaaaatttg aaagagaatg ggatagagag 180
ctggcttcaa agaaaaatcc taaactcatt aatgcccttc ggcgatgttt tttctggaga 240
tttatgttct atggaatctt tttatattta ggggaagtca ccaaagcagt acagcctctc 300
ttactgggaa gaatcatagc ttctatgac ccggataaca aggaggaacg ctctatcgcg 360

atztatctag	gcataggctt	atgccttctc	tttattgtga	ggacactgct	cctaçaccca	420
gccatttttg	gccttcatca	catttggaatg	cagatgagaa	tagctatggt	tagtttgatt	480
tataagaaga	ctttaaagct	gtcaagccgt	gttctagata	aaataagtat	tggacaactt	540
gttagtctcc	tttccaacaa	cctgaacaaa	tttgatgaag	gacttgcatt	ggcacatttc	600
gtgtggatcg	ctcctttgca	agtggcactc	ctcatggggc	taatctggga	gttgttacag	660
gcgtctgcct	tctgtggact	tggtttcctg	atagtccttg	ccctttttca	ggctgggcta	720
gggagaatga	tgatgaagta	cagagatcag	agagctggga	agatcagtga	aagacttggt	780
attacctcag	aaatgatcga	gaacatccaa	tctgttaagg	catactgctg	ggaagaagca	840
atggaaaaaa	tgattgaaaa	cttaagacaa	acagaactga	aactgactcg	gaaggcagcc	900
tatgtgagat	acttcaatag	ctcagccttc	ttcttctcag	ggttctttgt	ggtgttttta	960
tctgtgcttc	cctatgcact	aatcaaagga	atcatcctcc	ggaaaatatt	caccaccatc	1020
tcattctgca	ttgttctgcg	catggcggtc	actcggcaat	ttccctgggc	tgtacaaaca	1080
tggatgact	ctcttggagc	aataaacaaa	atacaggatt	tcttacaaaa	gcaagaatat	1140
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tgggaggagg	gatttgggga	attatttgag	aaagcaaaac	aaaacaataa	caatagaaaa	1260
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ggagcaggca	agacgagctt	gctcatgatg	atcatgggcg	agttagaacc	aagtgaaggc	1440
aagatcaaac	attccggccg	catcagcttt	tgcagccaat	tcagttggat	catgcccggt	1500
accatcaagg	agaacataat	cttcggcgctc	agttacgacg	agtaccgcta	tcgctcggtg	1560
attaaggcct	gtcagttgga	ggag				1584

<210> 102

<211> 323

<212> DNA

<213> Artificial Sequence

<220>

<223> Trans-splicing domain of CFTR PTM

<400> 102

gtaagatata	accgatatgt	gtctaacctg	attcgggcct	tcgatacgtt	aagatccacc	60
ggtcaaaaag	ttttcacata	atttcttacc	tcttcttgaa	ttcatgcttt	gatgacgctt	120
ctgtatctat	attcatcatt	ggaacaccca	atgatatttt	ctttaatggt	gcctggcata	180
atcctggaaa	actgataaca	caatgaaatt	cttccactgt	gcttaatttt	accctctgaa	240
ttctccattt	ctcccataat	catcattaca	actgaactct	ggaaataaaa	cccatcatta	300
ttaactcatt	atcaaatcac	gct				323

<210> 103

<211> 165

<212> DNA

<213> Artificial Sequence

<220>

<223> PTM binding domain

<400> 103

gctagcaata	atgacgaagc	cgccccctcac	gctcaggatt	cacttgccctc	caattatcat	60
cctaagcaga	agtgtatatt	cttatttgta	aagattctat	taactcattt	gattcaaaa	120
atttaaaata	cttctgtttt	cacctactct	gctatgcacc	cgcg		165

<210> 104
<211> 225
<212> DNA
<213> Artificial Sequence

<220>
<223> Trans-splicing domain of PTM

<400> 104
aataatgacg aagccgcccc tcacgctcag gattcacttg cctccaatt atcatcctaa 60
gcagaagtgt atattcttat ttgtaaagat tctattaact catttgattc aaaatattta 120
aaatacttcc tgtttcacct actctgctat gcaccgcgg aacattatta taacgttgct 180
cgaatactaa ctggtacctc ttcttttttt ttgatatcc tgcag 225

<210> 105
<211> 3069
<212> DNA
<213> Artificial Sequence

<220>
<223> CFTR PTM sequence

<400> 105
acttcacttc taatgatgat tatgggagaa ctggagcctt cagagggtaa aattaagcac 60
agtgaagaa tttcattctg ttctcagttt tcctggatta tgcctggcac cattaagaa 120
aataatcatct ttggtgtttc ctatgatgaa tatagataca gaagcgtcat caaagcatgc 180
caactagaag aggacatctc caagtttgca gagaaagaca atatagttct tggagaaggt 240
ggaatcacac tgagtggagg tcaacgagca agaatttctt tagcaagagc agtatacaaa 300
gatgctgatt tgtatttatt agactctcct tttggatacc tagatgtttt aacagaaaaa 360
gaaatatttg aaagctgtgt ctgtaaactg atggctaaca aaactaggat tttggctact 420
tctaaaatgg aacattttaa gaaagctgac aaaatattaa ttttgcataa aggttagcagc 480
tatttttatg ggacattttc agaactccaa aatctacagc cagacttttag ctcaaaactc 540
atgggatgtg attcttttcga ccaatttagt gcagaaagaa gaaattcaat cctaactgag 600
accttacacc gtttctcatt agaaggagat gctcctgtct cctggacaga aacaaaaaaa 660
caatctttta aacagactgg agagtgtggg gaaaaaagga agaattctat tctcaatcca 720
atcaactcta tacgaaaatt ttccattgtg caaaagactc ccttacaat gaatggcatc 780
gaagaggatt ctgatgagcc tttagagaga aggctgtcct tagtaccaga ttctgagcag 840
ggagaggcga tactgcctcg catcagcgtg atcagcactg gcccacgct tcaggcacga 900
aggaggcagt ctgtcctgaa cctgatgaca cactcagtta accaaggcca gaacattcac 960
cgaaagacaa cagcatccac acgaaaagtg tcaactggccc ctcaaggcaa cttgactgaa 1020
ctggatatat attcaagaag gttatctcaa gaaactggct tggaaataag tgaagaaatt 1080
aacgaagaag acttaaagga gtgctttttt gatgatatgg agagcatacc agcagtgact 1140
acatggaaca cataccttcg atatattact gtccacaaga gcttaatttt tgtgctaatt 1200
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gtgattatca ccagcaccag ttctgtattat gtgtttttaca tttacgtggg agtagccgac 1380
actttgcttg ctatgggatt cttcagaggt ctaccactgg tgcatactct aatcacagt 1440
tcgaaaattt tacaccacaa aatgtttacat tctgtttctc aagcacctat gtcaaccctc 1500
aacacgttga aagcaggtgg gattcttaat agattctcca aagatatagc aatttttgat 1560

gaccttctgc	ctcttaccat	atttgacttc	atccagttgt	tattaattgt	gattggagct	1620
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gcttttatta	tggtgagagc	atatttcctc	caaacctcac	agcaactcaa	acaactggaa	1740
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catactgcc	actggttctt	gtacctgtca	acactgcgct	ggttccaaat	gagaatagaa	1920
atgatttttg	tcattcttctt	cattgctgtt	accttcattt	ccattttaac	aacaggagaa	1980
ggagaaggaa	gagttggtat	tatcctgact	ttagccatga	atatcatgag	tacattgcag	2040
tgggctgtaa	actccagcat	agatgtggat	agcttgatgc	gatctgtgag	ccgagtcttt	2100
aagttcattg	acatgccaac	agaaggtaaa	cctaccaagt	caaccaaacc	atacaagaat	2160
ggccaactct	cgaaagttat	gattattgag	aattcacacg	tgaagaaaga	tgacatctgg	2220
ccctcagggg	gccaaatgac	tgtcaaagat	ctcacagcaa	aatacacaga	aggtggaaat	2280
gccatattag	agaacatttc	cttctcaata	agtcctggcc	agagggtggg	cctcttggga	2340
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ggagaaatcc	agatcgatgg	tgtgtcttgg	gattcaataa	ctttgcaaca	gtggaggaaa	2460
gcctttggag	tgataccaca	gaaagtattt	atTTTTTctg	gaacatttag	aaaaaacttg	2520
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agatctgtga	tagaacagtt	tcctgggaag	cttgactttg	tccttgtgga	tgggggctgt	2640
gtcctaagcc	atggccacaa	gcagttgatg	tgcttggcta	gatctgttct	cagtaaggcg	2700
aagatcttgc	tgcttgatga	accagtgct	catttggatc	cagtaacata	ccaaataatt	2760
agaagaactc	taaaacaagc	atttgctgat	tgcacagtaa	ttctctgtga	acacaggata	2820
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gattccatcc	agaaactgct	gaacgagagg	agcctcttcc	ggcaagccat	cagccccctcc	2940
gacaggggtga	agctcttttc	ccaccggaac	tcaagcaagt	gcaagtctaa	gccccagatt	3000
gctgctctga	aagaggagac	agaagaagag	gtgcaagata	caaggcttca	tcatcatcat	3060
catcattag						3069

<210> 106

<211> 131

<212> DNA

<213> Artificial Sequence

<220>

<223> Binding domain of mouse factor VIII PTM

<400> 106

ctcgagctta	cctgaactaa	tttttttagaa	tattaaaatc	ctaagctttt	atatctctat	60
ccctctatct	tttgctctct	atccaatttt	tattaactta	gacttttaaa	agaaacttat	120
gagaaaaatt	t					131

<210> 107

<211> 71

<212> DNA

<213> Artificial Sequence

<220>

<223> Spacer sequence of PTM

<400> 107

ccgcggaaca	ttattataac	gttgctcgaa	tactaactgg	tacctcttct	tttttttttg	60
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atatacctgca g

71

<210> 108

<211> 527

<212> DNA

<213> Artificial Sequence

<220>

<223> Chicken beta actin promoter sequences

<400> 108

```
ccatggtcga cgtagcccc acgtttctgct tcaactctccc catctccccc ccctccccac 60
ccccaatttt gtattttattt attttttaat tattttgtgc agcgatgggg gcgggggggg 120
ggggggggcg cgcgccaggc ggggcggggc ggggcgaggg gcggggcggg gcgagggcga 180
gaggtgcggc ggcagccaat cagagcggcg cgctccgaaa gttcctttta tcgcgagggc 240
gcggcggcgg cggccctata aaaagcgaag cgcgcggcgg ccgggagtcg ctgcgacgct 300
gccttcgccc cgtgcccaacc tccgcctcga gcttacctga actaattttt tagaatatta 360
aaatcctaag cttttatact cctatccctc tatcttttgc tctctatcca atttttatta 420
acttagactt taaaaagaaa cttatgagaa aaatttcgcg ggaacattat tataacgttg 480
ctcgaatact aactggtacc tcttcttttt tttttgatat cctgcag 527
```

<210> 109

<211> 169

<212> DNA

<213> Artificial Sequence

<220>

<223> Sequence not included in construct

<400> 109

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cgccgcctcg cgccgcccgc cccggctctg actgaccgcg ttactcccac aggtgagcgg 60
gcgggacggc ccttctcctc cgggctgtaa ttagcgcttg gtttaatcac ggcttgtttc 120
ttttctgtgg ctgcgtgaaa gccttgaggg gctccgggag gaattcgta 169
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<210> 110

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> F8 PTM sequences

<400> 110

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ggagtcgctg cgacgctgcc ttcgccccgt gccaacctcc gc
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42

<210> 111

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> F8 PTM sequences

<400> 111

ctcgagcacc gatatcgtaa ct

22

<210> 112

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> Exon 26, Flag tag, stop sequences of mouse factor
VIII PTM

<400> 112

gaggcccagc agcaatacga ctacaaggac gacgatgaca agtgagttaa aac

53

<210> 113

<211> 71

<212> DNA

<213> Artificial Sequence

<220>

<223> Spacer sequences of human or canine factor VIII
PTM

<400> 113

ccgcggaaca ttattataac gttgctcgaa tactaactgg tacctcttct tttttttttg
atatcctgca g

60
71